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Whole body cryotherapy, cold water immersion, or a placebo following resistance exercise: A case of mind over matter?

Authors: Laura J. Wilson¹, Lygeri Dimitriou¹, Frank A. Hills², Marcela B. Gondek² & Emma Cockburn³

¹ London Sports Institute, Middlesex University, Allianz Park, London, UK.

² Biomarker Research Group, Department of Natural Sciences, Middlesex University, London, UK.

³ Newcastle University, School of Biomedical Sciences, Newcastle upon Tyne, UK.

Corresponding Author:

Laura Wilson
London Sports Institute,
Middlesex University,
Greenlands Lane,
London,
NW4 1RL
UK
Email: Laurawilson1@live.com
Tel: 020 8411 5000

ABSTRACT

Purpose: The use of cryotherapy as a recovery intervention is prevalent amongst athletes. Performance of high volume, heavy load resistance exercise is known to result in disturbances of muscle function, perceptual responses and blood borne parameters. Therefore, this study investigated the influence of cold water immersion (CWI), whole body cryotherapy (WBC) or a placebo (PL) intervention on markers of recovery following an acute resistance training session.

Methods: Twenty four resistance trained males were matched into a CWI (10min at 10°C), WBC (3- and 4 min at -85°C) or PL group before completing a lower body resistance training session. Perceptions of soreness and training stress, markers of muscle function, inflammation and efflux of intracellular proteins were assessed before, and up to 72 h post exercise.

Results: The training session resulted in increased soreness, disturbances of muscle function, and increased inflammation and efflux of intracellular proteins. Although WBC attenuated soreness at 24 h, and positively influenced peak force at 48 h compared to CWI and PL, many of the remaining outcomes were trivial, unclear or favoured the PL condition. With the exception of CRP at 24 h, neither cryotherapy intervention attenuated the inflammatory response compared to PL.

Conclusion: There was some evidence to suggest that WBC is more effective than CWI at attenuating select perceptual and functional responses following resistance training. However, neither cryotherapy intervention was more effective than the placebo treatment at accelerating recovery. The implications of these findings should be carefully considered by individuals employing cryotherapy as a recovery strategy following heavy load resistance training.

Keywords: Muscle Damage; Muscle Function; Inflammation; Resistance training

Abbreviations

CK-M	Creatine Kinase-M
CMJ	Counter Movement Jump
CRP	C-Reactive Protein
CWI	Cold Water Immersion
DALDA	Daily Analysis of the Lifestyle Demands of Athletes
DXA	Dual X-ray Absorptiometry

ELISA	Enzyme-Linked Immunosorbent Assay
IL-6	Interleukin-6
MVIC	Maximal Voluntary Isometric Contraction
PL	Placebo
RFD	Rate of Force Development
RM	Repetition Maximum
RSI	Reactive Strength Index
TNF- α	Tumour Necrosis Factor- α
WBC	Whole Body Cryotherapy

INTRODUCTION

Exercise-induced muscle damage, most commonly resulting from unaccustomed or strenuous exercise, can lead to detrimental changes in perceptual responses, circulating intracellular proteins and functional capacity (Clarkson & Hubal, 2002). For athletes, any reduction in force producing ability, coupled with increases in muscle soreness could negatively impact upon subsequent training and performance (Khan et al., 2016). Therefore, the implementation of recovery interventions to expedite recovery is commonplace. Cryotherapy refers to the application of cold for therapeutic purposes, and its use as a means of accelerating recovery after strenuous exercise is becoming increasingly popular (Bleakley, Bieuzen, Davison, & Costello, 2014; Leeder, Gissane, van Someren, Gregson, & Howatson, 2012). Many top level athletes, coaches and practitioners have adopted cryotherapy as a potentially beneficial adjuvant to training. Whilst cold water immersion (CWI) remains an accessible modality requiring little equipment or specialist instruction, whole body cryotherapy (WBC) has been marketed as an alternative. There appears to be a perception that the extreme nature of WBC, which utilises far lower temperatures than CWI (-85°C to -125°C versus $10\text{-}15^{\circ}\text{C}$ respectively) can offer enhanced benefits for recovery (Bleakley et al., 2014). The use of WBC continues to grow, and in some cases appears to be replacing more traditional cold therapies such as CWI (Costello, Donnelly, Karki, & Selfe, 2014; Savic, Fonda, & Sarabon, 2013) for those individuals or teams who have access to the newer technology. There is a wealth of literature to suggest that CWI is effective at reducing delayed onset muscle soreness (DOMS) post exercise (Bleakley et al., 2012), but the influence on more functional markers of recovery such as strength, power and dynamic sporting movements remains less clear. Similarly, a review from Bleakley et al. (2014) found that whilst WBC can offer improvements in soreness and subjective recovery after exercise, there is little evidence of improvements in functional recovery.

Despite its growing popularity there is still very little available research directly comparing the different modalities or suggesting that WBC is any more effective than CWI as a recovery strategy following strenuous exercise. Abaïdia and colleagues (2016) compared the effectiveness of CWI and WBC on markers of recovery following an eccentric muscle damaging protocol. Their results showed that CWI was more effective for accelerating both functional and perceptual recovery post exercise compared to WBC. Whilst the findings add to the current body of literature, the unilateral eccentric exercise protocol used has little real world applicability to sports performance and therefore lacks ecological validity. Furthermore, muscle damaging exercise was carried out unilaterally, with conclusions about effectiveness based on bilateral vertical jump performance. A recent study

1 from Hohenauer and colleagues (2018) evaluated the effect of partial body cryotherapy and CWI on recovery
2 following 5 x 20 drop jumps. Their findings suggested that although there was no treatment effect for soreness or
3 functional recovery, there was a greater physiological response (assessed via cutaneous vascular conductance,
4 thigh muscle oxygen saturation and lower extremity skin temperature) for CWI compared to partial body
5 cryotherapy. These findings are supported by Mawhinney et al., (2017) who demonstrated that limb blood flow
6 is reduced to a greater extent following CWI than WBC. Further, research from our group has evaluated the
7 efficacy of CWI and WBC on performance following a trail marathon and found that WBC negatively impacted
8 the recovery of muscle function compared to CWI, and that neither intervention was more effective than a placebo
9 (Wilson et al., 2018). Presently, there do not appear to be any other studies directly comparing the effectiveness
10 of the two different cryotherapy modalities on functional recovery after resistance exercise.

11 Minett & Costello (2015) highlight the need for specificity in the prescription of recovery interventions. It is well
12 known that the mechanisms of muscle damage differ depending on the nature of the exercise stress (Armstrong,
13 Warren, & Warren, 1991); whilst long duration endurance exercise is likely to result in predominantly metabolic
14 damage (Tee, Bosch, & Lambert, 2007), resistance exercise can result in the breakdown of structural elements of
15 muscle tissue and potentially greater functional perturbations. Therefore, the effectiveness of any recovery
16 modality should be examined in relation to different exercise modes. The importance of resistance exercise as an
17 adjunct to more traditional sport specific skills training is becoming more evident in competitive sport (Bartolomei,
18 Hoffman, Merni, & Stout, 2014). Progressive, structured, heavy resistance training is no longer solely used by
19 bodybuilders and weightlifters but also by team sport players, dancers, gymnasts and swimmers (Crowley,
20 Harrison, & Lyons, 2017; Dowse, McGuigan, & Harrison, 2017). Therefore, it is pertinent to assess the influence
21 of cryotherapy on markers of recovery following resistance training. Moreover, there is still scope to explore
22 whether WBC and CWI exposures elicit different physiological responses and time courses of recovery (Hayter,
23 Doma, Schumann, & Deakin, 2016) following strenuous exercise.

24 Furthermore, there appears to be increasing evidence that many of the therapeutic effects attributed to cryotherapy
25 treatment may be due to a placebo effect (Broatch, Petersen, & Bishop, 2014; Wilson et al., 2018). Currently, the
26 vast majority of cryotherapy studies have been conducted using a control group, and have not taken expectance
27 effect or treatment belief into account when reporting study outcomes. Therefore, there is a need for future
28 investigations to evaluate cryotherapy treatments in comparison to an effectively administered placebo
29 intervention, rather than a control.

Hence, the main aim of this study was to compare the efficacy of CWI and WBC on recovery following strenuous resistance exercise, in order to try and address the current disparity in the literature. A further aim of this study was to use a holistic approach, encompassing performance, perceptual and blood borne markers, to establish whether either cryotherapy modality is any more effective than a placebo intervention following resistance exercise. It was hypothesised that CWI would be more beneficial for recovery than WBC, but that neither intervention would be more efficacious than a placebo treatment.

METHODS

Participants

A convenience sample of twenty four healthy male volunteers participated in this study (Table 1). Participants had no previous experience of cryotherapy and were required to have at least 12 months experience of strength training. All participants were non-smokers with no history of recent illness or lower limb injury. For 72 h prior to the baseline testing day and for the duration of the study, participants were asked to refrain from any additional strenuous exercise, and abstain from therapeutic treatments including massage and anti-inflammatory drugs, as well as any nutritional supplements.

INSERT TABLE 1 HERE

Study Design

All procedures were granted ethics approval by the Institutional committee according to the Helsinki declaration prior to testing. All participants received both written and verbal information about the purpose and potential risks of the proposed intervention. Participants gave their written informed consent and completed a comprehensive health questionnaire. Participants were matched into the placebo, CWI or WBC intervention group based on a ratio of their predicted 1RM back squat to lean mass assessed via DXA scan (fan beam, Lunar Prodigy 4, GE Medical Systems, Lunar, Madison, WI, USA) (Roberts, Raastad, et al., 2015). Participants were familiarised with all testing procedures at least 72 h before the baseline session. At baseline, measures of all dependent variables were recorded before completion of the training session. Immediately after the training session a further blood sample was collected, and within 15 min participants commenced their allocated recovery intervention. Participants were also required to give blood samples at 60 and 120 min post intervention. Participants returned

to the laboratory to repeat measurements of all dependent variables at 24, 48 and 72 h following completion of the resistance training session.

Daily Analysis of the Lifestyle Demands of Athletes (DALDA)

Stress reaction symptoms were recorded using the DALDA questionnaire, and data from part 'B' is presented. The questionnaire has been used previously to monitor alterations in stress response following strenuous exercise and cryotherapy treatment (Wilson et al., 2018).

Blood Sampling

Whole blood samples were collected from the antecubital vein into 4 mL vacutainers for the purpose of assessing muscle damage and inflammation. Blood samples were then centrifuged at 3000 rpm for 8 min before being aliquoted and stored at -80°C for later analysis of creatine kinase-M (CK-M), interleukin 6 (IL-6), C reactive protein (CRP) and tumour necrosis factor- α (TNF α). Blood samples were taken at baseline (CK-M, IL-6, CRP & TNF α), immediately post training (IL-6 and TNF α), 60 and 120 min post intervention (IL-6 and TNF α), 24 (CK-M, IL-6, CRP & TNF α), 48 and 72 h post (CK-M, CRP & TNF α) post intervention (Leeder et al., 2014).

CK-M

Plasma CK-M concentrations were measured by simple step enzyme-linked immunosorbent assay (ELISA) (Abcam, Cambridge, UK). The reported assay ranges are 0.03 – 2.0 U/L, the minimum detection concentration (MDC) is 0.014 U/L, and the human serum intra- and inter-assay CVs were 3 and 9%, respectively.

IL-6

Plasma IL-6 concentration was determined using a quantitative sandwich (QS) ELISA (Quantikine, R&D Systems Europe Ltd., Abingdon, UK). The reported assay ranges are 3.1 - 300 pg/ml, the MDC is 0.7 mg/pl, and the intra- and inter-assay CVs were 2 and 3.8% respectively.

CRP

Plasma CRP concentration was determined using a QS ELISA technique (IBL International GmbH, Hamburg, Germany). The MDC for the assay was <1 μ g/ml with an intra and inter-assay CV of 5.12 and 14.3% respectively.

TNF- α

Plasma TNF- α concentration was measured by QS-ELISA (BioVendor, Brno, Czech Republic). The reported assay ranges are 7.8 – 500 pg/ml, the MDC is 2.3 pg/ml, and the intra and inter-assay CVs were 6.0 and 7.4% respectively.

Perceived Soreness

Participants indicated their perceived muscle soreness of the lower limbs during a body weight squat (approx. knee angle of 90°) using a 0 (no soreness on movement) to 10 (muscles too sore to move) Likert scale. This method has been used successfully in previous studies to monitor changes in perceptions of pain following exercise (Vaile, Gill, & Blazeovich, 2007).

Peak Torque and Isometric Contractions

Peak knee extensor torque and maximal voluntary isometric contraction (MVIC) were measured on the right limb using an isokinetic dynamometer (Biodex 3, Biodex Medical Systems, Shirley, NY, USA). Following a standardised warm-up, participants performed three x 3 sec MVICs of the knee extensors at a knee angle of 90° in accordance with previous studies (de Ruitter, van der Linden, van der Zijden, Hollander, & de Haan, 2003). Participants were then required to perform 3 maximal isokinetic efforts of the knee flexors and extensors at 60 deg·s⁻¹. Participants were encouraged to work as fast and as hard as possible against the resistance of the dynamometer arm throughout the full range of motion. The peak values were used for analysis.

Reactive Strength Index (RSI)

Participants dropped from a platform at a height of 30 cm onto a portable force plate (Kistler, Switzerland) and then jumped vertically for maximum height as quickly as possible. Emphasis was placed on minimum ground contact time, whilst maintaining maximum jump height. Participants kept their hands on their hips for the duration of the movement, and performed 3 maximal jumps at each testing point. Reactive strength index (RSI) for each effort was calculated by dividing flight time by ground contact time (Flanagan & Comyns, 2008) and peak RSI values were used for statistical analysis.

Counter Movement Jump (CMJ)

From a relaxed standing position on a portable force platform (Kistler, Switzerland), participants made a countermovement to a squat position (self-selected depth) before jumping vertically for maximal height. Each jump was performed in a continuous movement with hands remaining on hips for the duration. Three jumps were

recorded at each testing session. Any efforts that deviated from the prescribed technique were deemed void and repeated. Raw data was analysed in accordance with Chavda et al. (2017), and peak jump height values from each testing session were used for statistical analysis.

Isometric Squat

Isometric squat parameters were measured using a portable force platform (Kistler, Switzerland), interfaced with a laptop and placed inside a custom designed rack (Absolute Performance, Cardiff, UK) allowing for adjustable bar height. For each participant, the bar was set in line with the base of their sternum, in an attempt to ensure that the isometric squat was performed in the mid-range of a back squat movement. The bar position was replicated at each testing session. Participants were asked to maintain a stable position under the bar whilst applying minimal pressure. Participants were asked to drive straight up as fast and as hard as possible against the bar and to maintain the contraction for 3 sec (Roberts et al., 2014). Three trials were completed at each testing session with a 3 min rest between efforts. If there was any sign of a visible countermovement, the trial was deemed void and repeated after a 3 min rest. Rate of force development was calculated from the force–time curve as the slope of the linear function from 100 to 200 milliseconds. Changes in the early phase of a contraction (<100 ms) can be attributed to fatigue or other neural factors, whilst changes in the later phase (>100 ms) tend to reflect alterations to contractile elements of skeletal muscle (Maffiuletti et al., 2016; Peñailillo, Blazevich, Numazawa, & Nosaka, 2015). The isometric peak force was determined as the maximal force recorded from each trial minus body mass. Peak isometric force was taken and used for analysis. The peak RFD value from 100-200 ms was used for analysis.

Exercise Protocol

At the familiarisation session, predicted 1RM for the back squat, split squat, barbell hip thrust and Romanian deadlift was calculated for each participant. After completing a thorough warm up, participants were asked to select a load which they believed would elicit fatigue in 10 or fewer repetitions before being instructed to complete as many repetitions as possible. Loss of technique during any exercise was deemed as an unsuccessful lift. If the number of successful lifts exceeded 10 repetitions, participants rested for 15 min before attempting the exercise with an increased load. This was repeated for each of the 4 exercises and predicted 1RM was calculated using the Wathen prediction equation (Wathen, 1994). For the resistance training session, all exercises were performed at 80% of the predicted 1RM for each exercise. The training session comprised 4 sets of 6 reps of back squats, 4 sets of 8 reps of split squats, 4 sets of 8 reps of hip thrusts and 4 sets of 8 reps of Romanian deadlifts. This represented a total volume of 120 repetitions which is comparable to other studies utilising resistance exercise

and/or plyometrics to investigate recovery (Byrne & Eston, 2002; Jakeman, Byrne, & Eston, 2010), but offers a more ecologically valid exercise model to examine the efficacy of cryotherapy (Minett & Costello, 2015). Fifteen minutes after cessation of exercise, participants were asked to record a session RPE (Day, McGuigan, Brice, & Foster, 2004) (Table 1.)

Interventions

Whole Body Cryotherapy

The WBC group were exposed to 2 cold treatments in a cryotherapy chamber (BOC, London, UK). Participants (up to 2 at a time) spent 3min in the chamber set to $-85^{\circ}\text{C} \pm 5^{\circ}\text{C}$. Participants then had a 15min warming period in an ambient room before entering the chamber for a further 4min bout at $-85^{\circ}\text{C} \pm 5^{\circ}\text{C}$ (Wilson et al., 2018). Before entering the chamber participants were asked to remove glasses, contact lenses and any jewellery or piercings. During exposure, participants wore a pair of shorts and nothing above the waist, gloves, dry socks and shoes, a hat covering the ears and a mask to protect the nose and mouth.

Cold Water Immersion

Immediately after cessation of exercise participants sat in a mobile ice bath (iSprint Twin, iCool, Cranlea, UK) ensuring their lower limbs and iliac crest were fully immersed. Participants remained in the ice bath filled with water cooled to 10 degrees ($\pm 0.5^{\circ}$) for 10 min. The ice bath was connected to a chiller unit (MiCool, iCool, Cranlea, UK) so that water temperature could be monitored and maintained within the desired parameters for the duration of the treatment. During exposure participants wore shorts and immediately after they were asked to towel themselves dry and change into clean, dry clothing. This protocol is comparable to those utilised in other single exposure studies examining the effects of CWI on various measures of recovery (Ascensão, Leite, Rebelo, Magalhães, & Magalhães, 2011; Roberts et al., 2014).

Placebo

As it was not possible to blind participants to their recovery intervention, a placebo, rather than a control group was used. Branched chain amino acids (BCAAs) are commonly used by athletes and have been shown to accelerate recovery following resistance training (Norton & Layman, 2006). Therefore, participants in the placebo group were given a cornstarch pill and informed that they were taking a BCAA supplement after the training session. Participants were asked to rest quietly for 10 min following completion of the training session. It was

hoped that the use of a placebo (sham) group would minimise associated placebo effects (i.e. effects of the treatment that were not related to the treatment itself) (McClung & Collins, 2007).

Statistical Analysis

Confidence limits (CL) and magnitude based inferences were calculated for each dependent variable using methods described by Batterham and Hopkins (2006). The smallest practically worthwhile effect for muscle function and blood parameters was the smallest standardised (Cohen) change in the mean: 0.2 times the between-subject SD for baseline values of all participants (Batterham & Hopkins, 2006). The smallest worthwhile change for muscle soreness and DALDA scores was a change in raw values of 1.0 (Hopkins, 2015). In order to account for large inter-individual differences in blood parameters, baseline values were used as a covariate. Qualitative descriptors relate to the likelihood of increased, trivial or decreased outcomes. Clinical inferences were based on threshold chances of harm and benefit of 0.5 and 25% respectively. In cases where the inference was unclear, a beneficial inference was reported where the odds ratio of benefit/harm was greater than 66. In order to overcome heteroscedastic error, the analysis of dependent variables was conducted on log-transformed data (Nevill & Lane, 2007), except in the cases of muscle soreness and DALDA. Interval scaling makes it inappropriate to log-transform data for these variables (Nevill & Lane, 2007) so analysis was conducted on raw values. Each dependent variable was analysed using a published spreadsheet by Hopkins (2015). Changes are reported as percentages for function variables, raw changes for perceptual variables and factor changes for blood markers. Effect sizes are reported in addition to magnitude based inferences, where 0.0-0.19 is trivial, 0.20-0.59 is small, 0.60-1.19 is moderate, 1.20-1.99 is large, 2.0-3.99 is very large and 4.0+ is extremely large (Hopkins, Marshall, Batterham, & Hanin, 2009). P values for the main interaction effects (time x group), determined using a factorial ANOVA with repeated measures on 1 factor (time), have also been stated. When the main effect was significant, an LSD adjusted post-hoc test was used to investigate between-group differences at specific time points.

Results

The outcomes for changes over time as well as group comparisons for all parameters can be seen in tables 2 and 3, and figure 1. The resistance exercise session resulted in increased perceptions of soreness and stress reaction symptoms, decreases in muscle function and increases in markers of structural damage and inflammation.

DALDA

At baseline, DALDA values were 4 ± 6 , 1 ± 1 and 2 ± 2 scores marked as worse than normal for placebo, CWI and WBC respectively. Scores marked worse than normal peaked at 24 h for the placebo group and at 48 h for both cryotherapy groups. CWI demonstrated greater increases compared to placebo at all time points. Scores were greater for WBC compared to the placebo at 48 h, but demonstrated a beneficial effect compared to the placebo at 24 h. All other group comparisons were trivial or unclear. The p value for the main interaction effect was 0.742.

Perceived soreness

At baseline, soreness values were 1 ± 1 , 1 ± 1 and 2 ± 2 (VAS 0-10) for placebo, CWI and WBC respectively. Perceptions of soreness increased in all groups; scores remained elevated in the placebo and CWI groups, but returned to baseline levels in the WBC group at 72 h post. WBC elicited smaller increases compared to both placebo and CWI at 24 h, but comparisons were unclear at 48 and 72 h post. CWI demonstrated a trivial effect compared to placebo at all time points. The p value for the main interaction effect was 0.061.

INSERT TABLE 2 HERE

Peak Torque and Isometric Contractions

MVIC 90°

At baseline, MVIC values at 90° were 273.60 ± 57.76 , 255.00 ± 63.17 and 240.59 ± 69.74 N for placebo, CWI and WBC respectively. MVIC was reduced at all time points in all groups. CWI demonstrated greater decrements compared to placebo at 24 and 48 h post, whilst WBC was trivial compared to placebo at 24 h. Comparisons between CWI and WBC were unclear at all time points. The p value for the main interaction effect was 0.714.

Peak Torque 60deg·s⁻¹

At baseline, peak torque values at 60deg·s⁻¹ were 223.54 ± 50.65 , 207.18 ± 38.85 and 194.98 ± 37.61 for placebo, CWI and WBC respectively. Changes in peak torque values at 60deg·s⁻¹ for the placebo group were trivial at all time points, but demonstrated a decrease in both cryotherapy groups between baseline and 24 h, and decreases or trivial changes between baseline and 48 h and baseline and 72 h. Group comparisons demonstrated that at 24 h, values for both CWI and WBC were reduced compared to the placebo group, as a result of trivial changes in the placebo group. The p value for the main interaction effect was 0.054.

RSI

At baseline, RSI values were 1.80 ± 0.28 , 2.20 ± 0.31 and 2.07 ± 0.31 $\text{cm}\cdot\text{s}^{-1}$ for placebo, CWI and WBC respectively. For the placebo and CWI groups, all changes over time demonstrated decreased or unclear effects, and for WBC, there was a possible improvement at 24 h post, but a decrease at both 48 and 72 h post. Cryotherapy was unclear, or less effective compared to placebo at all time points, with the exception of WBC at 24 h which showed a likely improvement. The p value for the main interaction effect was <0.001 . Post-hoc analyses revealed significant differences between WBC and placebo, and WBC and CWI at 24 h ($p < 0.05$).

CMJ

At baseline, CMJ height values were 0.35 ± 0.06 , 0.34 ± 0.04 and 0.40 ± 0.05 m for placebo, CWI and WBC respectively. The exercise bout resulted in decreased CMJ performance for all groups at all time points. The greatest decrements in performance were evident at 24 h post for placebo and WBC, and at 48 h post for CWI. In terms of group comparisons, WBC demonstrated a greater decrement compared to CWI at 24 h, but unclear, and trivial effects at 48 and 72 h respectively. When compared to the placebo intervention, CWI showed greater decrements at 48 and 72 h, whilst WBC showed greater decrements at both 24 and 72 h post. The p value for the main interaction effect was 0.714.

Isometric squat

Isometric Peak Force

At baseline isometric peak force values were 1620.43 ± 330.01 , 1693.36 ± 398.76 and 1763.01 ± 682.02 Nm for placebo, CWI and WBC respectively. Peak performance perturbations were evident at 48 h post for all groups. All group comparisons at 24 and 72 hours were either unclear or trivial. However, at 48 h CWI showed a reduction compared to placebo, and WBC was improved compared to CWI and placebo. The p value for the main interaction effect was 0.018. Post-hoc analyses revealed significant differences between CWI and WBC at 48 h ($p < 0.05$).

RFD 100-200ms

At baseline, RFD values between 100 and 200 ms were 4866.78 ± 1889.46 , 5022.59 ± 1081.36 and 4135.02 ± 1756.94 $\text{Nm}\cdot\text{s}^{-1}$ for placebo, CWI and WBC respectively. Decrements in performance were most pronounced at 24 h for WBC, and at 48 h for placebo and CWI. WBC demonstrated an improvement compared to CWI and placebo at 48 h, but comparisons were unclear at 72 h. WBC demonstrated a reduction in performance compared to the placebo at 24 h, and performance in the CWI group was reduced compared to the placebo at all time points.

The p value for the main interaction effect was <0.001 , although post-hoc analyses revealed no significant group interactions.

INSERT TABLE 3 HERE

Bloods

CK-M

At baseline, CK-M values were 79.7 ± 27.6 , 145.7 ± 184.8 and 253.2 ± 249.9 U/L for placebo, CWI and WBC respectively. Increases were most pronounced at 24 h in all groups (most likely very large (4.66; $x/\div 1.21$), most likely large (4.02; $x/\div 1.63$) and most likely moderate (4.63; $x/\div 1.41$) increases for PL, CWI and WBC respectively), and had not returned to baseline levels by 72 h in any group. Comparisons for the CWI group were unclear compared to placebo at 24 and 48 h, but demonstrated a possibly small increase at 72 h (1.20; $x/\div 1.45$). WBC demonstrated a trivial effect compared to placebo at 24 h, but a possibly moderate (1.44; $x/\div 1.69$) and likely large (1.57; $x/\div 1.40$) increase at 48 and 72 h respectively. For comparison between cryotherapy modalities, WBC demonstrated a possibly small (1.15; $x/\div 1.73$), likely moderate (1.61; $x/\div 1.94$), and possibly moderate (1.31; $x/\div 1.51$) increase compared to placebo at 24, 48 and 72 h respectively. The p value for the main interaction effect was 0.457.

IL-6

At baseline, IL-6 values were 778.4 ± 2015.8 , 25.9 ± 27.2 and 16.5 ± 27.8 pg/ml for placebo, CWI and WBC respectively. Change over time revealed trivial effects for all groups at all time points with the exception of WBC immediately- and 120 min post, where there were possibly small increases (1.78; $x/\div 1.78$ and 1.76; $x/\div 1.53$ respectively). All group comparisons were trivial at all time points. The p value for the main interaction effect was 0.437.

CRP

At baseline, CRP values were 1567.1 ± 2861 , 1126.4 ± 1071.9 and 358.4 ± 220.8 $\mu\text{g/ml}$ for placebo, CWI and WBC respectively. From baseline to 24 h, change over time analyses revealed a very likely small (2.43; $x/\div 1.54$) and possibly likely small (1.29; $x/\div 1.26$) increase for PL and CWI respectively whilst WBC demonstrated a very likely moderate increase (1.95; $x/\div 1.51$). At 48 h, both PL and CWI revealed a trivial change, whilst WBC demonstrated a likely moderate increase (2.06; $x/\div 1.65$). At 72 h PL and CWI demonstrated an unclear effect

whilst there was a possibly moderate increase (1.51; $x/\div 1.69$) for WBC. From baseline to 24 h CWI values demonstrated a likely large decrease compared to placebo (0.53; $x/\div 1.59$), whilst comparisons at 48 and 72 h were unclear. WBC demonstrated an unclear effect compared to placebo at 24 h, but a possibly moderate increase at 48 (1.53; $x/\div 1.85$) and 72 h (1.62; $x/\div 2.00$). WBC demonstrated a likely moderate increase compared to CWI at all time points (1.52; $x/\div 1.56$, 2.04; $x/\div 1.88$ and 1.89; $x/\div 1.86$ at 24, 48 and 72 h respectively). The p value for the main interaction effect was 0.377.

TNF- α

At baseline, TNF- α values were 38.7 ± 28.6 , 35.7 ± 24.6 and 32.1 ± 34.7 pg/ml for placebo, CWI and WBC respectively. The time course of response differed amongst groups; peak values were recorded at 120 min, 72 h and 48 h post for placebo, CWI and WBC respectively. Change over time analyses revealed unclear or trivial effects for PL at all time points. CWI showed a small increase immediately post (1.39; $x/\div 1.92$), an unclear, and then trivial change at 60 and 120 min. There was a likely moderate decrease for CWI at 24 h (0.39; $x/\div 2.71$), an unclear change at 48 h and a likely moderate increase (1.90; $x/\div 1.84$) at 72 h. Changes for WBC were trivial or unclear at all time points with the exception of a possibly small increase (1.60; $x/\div 1.99$) immediately post and a likely small increase (1.85; $x/\div 1.91$) at 48 h. CWI demonstrated a likely moderate increase (2.23; $x/\div 3.59$) compared to placebo immediately post, and a possibly small (1.48; $x/\div 3.62$), and likely moderate (2.43; $x/\div 2.15$) increase compared to placebo at 48 and 72 h respectively. Compared to placebo, WBC demonstrated a likely moderate increase (2.56; $x/\div 3.640$) immediately post, a possibly small increase (1.52; $x/\div 2.73$) at 60 min post and a likely large increase (3.94; $x/\div 3.51$) at 48 h. Compared to CWI, WBC demonstrated a possibly trivial increase (1.15; $x/\div 2.40$) immediately post, a possibly small increase (1.41; $x/\div 3.55$) at 60 min, and a likely moderate increase at 120 min (2.59; $x/\div 5.04$), 24 h (2.86; $x/\div 4.17$) and 48 h (2.66; $x/\div 2.46$). All other group comparisons were unclear. The p value for the main interaction effect was 0.553.

INSERT FIGURE 1 HERE

Where there are large differences in baseline values between groups, this is attributed to one or two individuals who had values substantially greater than the normal range. However, as data was covariates using baseline values and results are analysed as the difference between groups in change over time, these participants were not removed from the analysis.

DISCUSSION

1 The present study examined the effectiveness of a single bout of CWI or WBC, or a placebo intervention on
2 markers of recovery in resistance trained males following a high volume, heavy load lower body resistance
3 training session. The training session resulted in perturbations of muscle function, increases in perceptions of
4 soreness and stress response symptoms and increases in blood borne markers of damage and inflammation.
5 Overall, the results demonstrated little evidence to suggest that either cryotherapy intervention was more effective
6 than a placebo at limiting decrements in muscle function, perturbations in perceptual responses or increases in
7 inflammatory markers. Similarly, the majority of comparisons between CWI and WBC showed trivial or unclear
8 results, although there was some evidence to suggest that WBC is more effective than CWI at attenuating
9 detrimental increases in perceptual responses 24 post exercise, and that CWI may have greater potential for
10 reducing inflammation compared to WBC.

11 For both cryotherapy interventions, DALDA scores were unclear, trivial or increased compared to the placebo
12 intervention at all time points. However, from baseline to 24 h, WBC demonstrated a likely beneficial effect
13 compared to CWI. These findings are supported by Wilson et al., (2018) who reported that whilst neither CWI or
14 WBC offered any perceptual benefit over a placebo intervention, WBC was superior to CWI when monitoring
15 recovery following a marathon. These findings lend further support to the suggestion that many of the therapeutic
16 effects attributed to cryotherapy interventions may in fact be ascribed, at least in part, to a placebo effect (Broatch et
17 al., 2014). In terms of muscle soreness, CWI showed a trivial effect compared to the placebo intervention at all
18 time points, but from baseline to 24 h WBC was likely beneficial compared to both the placebo and CWI condition.

19 Maximal isometric strength at 90° decreased in all groups following completion of the resistance training session
20 and remained diminished at 72 h. Group comparisons revealed trivial or unclear effects of WBC compared to
21 placebo and CWI at all time point. For MVIC at 90°, CWI demonstrated moderate and small reductions compared
22 to placebo at 24 and 48 h respectively. Similarly, in terms of peak force assessed via maximal isometric squats,
23 despite all group comparisons being unclear at 24 and 72 h, CWI demonstrated a large performance reduction
24 compared to moderate reduction in the placebo group at 48 h. These findings are in contrast to Vaile, Halson, Gill,
25 & Dawson, (2008) who reported smaller peak force performance decrements in the CWI group (-7.3%) compared
26 to a passive recovery group (-15.7%) following a DOMS-inducing eccentric leg press protocol. Methodological
27 differences may help to explain the opposing findings. In the present study, participants completed a higher
28 volume training session (120 versus 70 repetitions) which may have resulted in greater muscle damage, evidenced
29 by greater peak force decrements at 48 h (-29.8 vs -7.3% for CWI and -18.8 vs -15.7% for placebo/control).

Secondly, the CWI intervention used in the study by Vaile and colleagues (2008) implemented a 14 min 15°C protocol whereas the present study utilised a 10 min 10°C protocol. This reaffirms the recommendation from Machado and colleagues (2016) that CWI at a temperature between 11 and 15°C for 11–15 min may provide the best results for both immediate and delayed effects. Further, as is becoming more important in cryotherapy literature (Broatch et al., 2014; Wilson et al., 2018), the present study employed a placebo, rather than a control group which may strengthen the study design and provide greater ecological validity. RFD is considered a more specific and sensitive indirect measure (Maffiuletti et al., 2016; Peñailillo et al., 2015) of muscle damage after exercise than MVIC. The RFD data from 100-200 ms largely mirrors the peak force data, suggesting that WBC was most beneficial at 48 h compared to CWI and placebo. However, unlike the peak force data, WBC demonstrated a reduced effect compared to the placebo at 24 h, so without further data the potential beneficial effects of WBC on peak force and RFD at specific time points should be interpreted cautiously.

For peak torque at 60 deg·s⁻¹ both cryotherapy interventions attenuated recovery compared to the placebo at 24 h. Further, CWI demonstrated a reduced recovery response compared to the placebo at 48 h. Comparisons between CWI and WBC were trivial or unclear at all time points, which is in contrast to Wilson et al., (2018) who found that recovery in WBC was reduced compared to CWI following a trail marathon. The selection of any outcome variable utilised to assess recovery after exercise should be specific to the exercise stress itself, and a time trial (although methodologically challenging) may have been more appropriate in the previous investigation. For this reason, peak torque values reported in the previous study may not accurately represent performance decrements following a prolonged endurance exercise stress.

Cryotherapy had a trivial or reduced impact on recovery of CMJ compared to the placebo at all time points. However, at 24 h WBC was possibly reduced compared to CWI, and this finding is supported by Abaïdia et al., (2016) who reported that there was a very likely moderate effect in favour of CWI for CMJ recovery compared to WBC 72 h after exercise. A recent investigation from Hohenauer et al., (2018) demonstrated that there was no difference between CWI and partial body cryotherapy for functional recovery assessed via MVCs and vertical jumps. However, it is worth noting that neither study employed a placebo or control condition, so recommendations relating to the efficacy of cryotherapy should be interpreted with caution. Furthermore, differing exercise stresses (dynamometry and repeated drop jumps respectively) make it difficult to directly compare findings to the present investigation. In terms of RSI derived from the drop jump data, both cryotherapy interventions demonstrated a reduced or unclear effect compared to the placebo intervention. However, in contrast

1 to the jump height data, WBC was most likely beneficial compared to CWI at 24 h. This result may indicate the
2 influence of a learning effect from baseline to the 24 h post testing session. Change over time analyses show that
3 RSI values in the WBC group demonstrated a possibly beneficial effect at 24 h, whereas there was a decrease in
4 both the placebo and CWI group at the same time point.

5 The finding that cryotherapy was ineffective at attenuating increases in CK following exercise is supported by
6 Jakeman, Macrae & Eston, (2009) who reported that despite peaking 24 h following plyometric exercise, there
7 were no differences in CK between the CWI and control group. Similarly, the results are supported by Wilson et
8 al., (2018) who reported that following completion of a trail marathon WBC was less effective than CWI at
9 tempering increases in CK.

10 A key mechanism purported to support the use of cryotherapy as a recovery intervention is that it can modulate
11 blood flow and cell metabolism (Mawhinney et al., 2017), resulting in an attenuated inflammatory response
12 (Tipton, Collier, Massey, Corbett, & Harper, 2017). The results from the present study do not support this premise,
13 with cryotherapy largely trivial or less effective compared to the placebo intervention. In line with previous
14 research, IL-6 peaked immediately post exercise (Roberts et al., 2014), however, all group comparisons were
15 trivial, suggesting very little difference between interventions. Given that IL-6 is an acute phase inflammatory
16 marker that often peaks immediately post exercise, it is possible that cryotherapy applied following exercise can
17 have little impact on circulating levels. This is in line with Selfe et al., (2014) who reported that a single WBC
18 exposure, irrespective of duration (1, 2 or 3 min), did not significantly alter circulating IL-6 following a game of
19 rugby league. The results from the CRP and TNF- α analyses demonstrated that CWI may offer slight benefits
20 compared to WBC, but that there was no benefit of cryotherapy compared to the placebo intervention. These
21 findings are supported by White, Rhind, & Wells, (2014) who reported that CWI (10° x 10 min) following high
22 intensity exercise does not reduce plasma markers of inflammation, and that prolonged CWI (10° x 30 min) can
23 actually exacerbate the inflammatory response. Similarly, previous research has suggested that ‘severe cold’
24 immersion protocols (5-10°) can negatively impact upon recovery, by eliciting a cold related stress response
25 (Machado et al., 2016). This in turn could escalate the inflammatory cascade response, increase perceptions of
26 soreness and ultimately impact on functional recovery (Machado et al., 2016; Wilson et al., 2018).

27 Potential limitations of the current study should also be addressed. The WBC treatment temperature utilised in the
28 present study was considerably warmer than that normally reported in the literature (-85° versus -110° to -140°),
29 therefore, although the findings add to the current body of literature, the findings cannot be generalised to colder

exposure temperatures. Secondly, there were large variations in baseline values for a number of outcome measures. For the blood markers, all results are reported as factor change over time and baseline values were used as a covariate. All participants avoided strenuous exercise for a minimum of 48 h before the baseline session, and it is likely that large variations are present in physically active populations. The pattern and magnitude of change was not largely different in participants who had large baseline values, compared to those with lower values. Participants were matched into groups based on lean mass and predicted 1RM, and as a result there were differences in absolute strength between groups. However, all functional outcomes were reported as percentage change to minimise the potential confounding effect of absolute raw values. Lastly, there was no direct measure of expectance effect or treatment belief in the present study. The authors acknowledge this as a limitation and appreciate that inclusion of this information may have strengthened the findings.

CONCLUSION

When comparing the efficacy of the different cryotherapy modalities on recovery following resistance training, although WBC demonstrated some beneficial effects compared to CWI, comparisons were largely unclear, trivial or favoured the CWI condition. These findings, in addition to those from Abaïdia et al., (2016) and Wilson et al., (2018) add more weight to the argument that WBC offers few additional benefits over CWI for recovery following strenuous exercise. Similarly, in terms of investigating the contribution of a potential placebo effect associated with cryotherapy, the majority of group comparisons revealed unclear, trivial or unfavourable effects of cryotherapy compared to the placebo intervention, contradicting much of the previous literature. Again, this echoes the findings from Wilson et al., (2018) and highlights the need for future cryotherapy studies to implement an effective placebo controlled design. Similarly, further research is warranted to better understand treatment belief and expectance effects amongst athletes prior to implementing any recovery strategy. By using a more ecologically valid exercise stress than some of the previous resistance exercise literature (Fulford, Eston, Rowlands, & Davies, 2015; McLeay et al., 2012), it is hoped that the results may be more applicable to real world scenarios.

Conflicts of Interest and Source of Funding

No external funding was received for this work. The authors declare no conflict of interest.

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Table 1. Participant characteristics

	<i>n</i>	Age (y)	Height (m)	Mass (kg)	Predicted 1RM (kg)	Lean mass (kg)	1RM/Lean mass	sRPE
PL	8	25.88 ± 5.19	1.80 ± 0.04	84.88 ± 13.81	125 ± 19.6	63.83 ± 7.51	1.95 ± 0.15	7.50 ± 1.41
CWI	8	21.88 ± 3.40	1.79 ± 0.05	84.39 ± 14.22	126 ± 21.3	66.56 ± 6.29	1.89 ± 0.22	7.63 ± 1.41
WBC	8	26.50 ± 8.40	1.71 ± 0.06	70.92 ± 10.20	120 ± 46.1	58.44 ± 6.49	2.04 ± 0.69	7.50 ± 1.07

Values are presented as mean \pm SD

1RM, 1 Repetition Maximum; sRPE, session rate of perceived exertion

Table 2. Change over time and group comparisons for perceptual markers

		Changes				Effects	
		Mean; \pm CL				Mean ^a ; \pm CL ^b	
		Qualitative outcome				Qualitative Outcome	
		Placebo	CWI	WBC	PL/CWI	PL/WBC	CWI/WBC
DALDA	B – 24h	0.38; \pm 3.3	1.5; \pm 0.9	-0.38; \pm 0.9	1.12; \pm 3.4	-0.76; \pm 3.4	-1.88; \pm 1.2
		Very large \uparrow^*	Large \uparrow^{**}	Trivial **	Small \uparrow^*	Unclear	Moderate \downarrow^{**}
	B – 48h	-0.25; \pm 2.4	1.63; \pm 1.1	0.5; \pm 2.5	1.88; \pm 2.6	0.75; \pm 3.2	-1.13; \pm 2.6
		Unclear	Large \uparrow^{**}	Small \uparrow^*	Moderate \uparrow^*	Small \uparrow^*	Unclear
	B – 72h	-1.13; \pm 2.8	0.13; \pm 0.2	-0.75; \pm 1.7	1.26; \pm 2.8	0.38; \pm 3.1	-0.88; \pm 1.7
		Unclear	Trivial ****	Unclear	Small \uparrow^*	Trivial *	Unclear
DOMS	B – 24h	3.88; \pm 1.4	3.75; \pm 1.4	0.63; \pm 2.1	-0.13; \pm 1.8	-3.25; \pm 2.4	-3.12; \pm 2.1
		Very large \uparrow^{****}	Very large \uparrow^{****}	Small \uparrow^*	Trivial *	Large \downarrow^{**}	Large \downarrow^{**}
	B – 48h	3.50; \pm 1.4	4.00; \pm 1.8	0.88; \pm 2.4	0.50; \pm 2.1	-2.62; \pm 2.6	-3.12; \pm 2.8
		Very large \uparrow^{***}	Very large \uparrow^{***}	Small \uparrow^*	Trivial *	Unclear	Unclear
	B – 72h	1.63; \pm 1.1	1.63; \pm 1.6	-0.25; \pm 2.0	0; \pm 1.8	-1.88; \pm 2.2	-1.88; \pm 2.4
		Large \uparrow^{**}	Large \uparrow^{**}	Trivial *	Trivial *	Unclear	Unclear

CL, confidence limit. Qualitative outcome represents the likelihood that the true value will have the observed magnitude represented by the number of asterisks (*) with *possibly, **likely, ***very likely and **** most likely.

^aMean represents the second named group minus the first named group.

^b90%CL – add and subtract this number to the mean to obtain the 90% confidence limits for the true difference

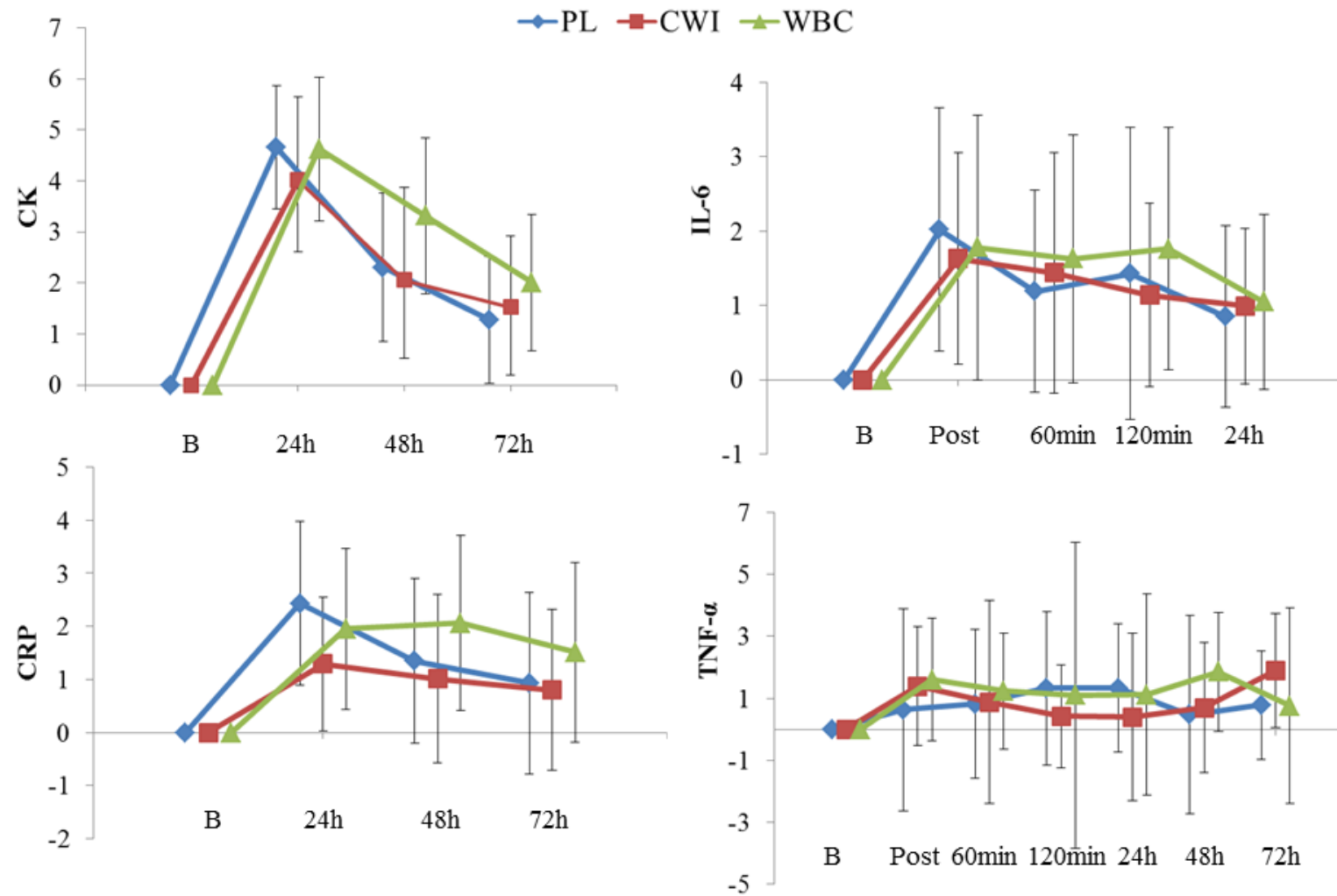


Figure 1. Factor change in blood variables with 90% CL error bars.